Signaling Pathways That Regulate Normal and Aberrant Red Blood Cell Development.

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Public Summary:
Blood cell development is controlled by cells and its environment. This review describes the signals that drive blood stem cells to mature and divide. These signals are important to maintain normal blood cell development. If the cells or signals are abnormal, they lead to diseases of blood cells including bone marrow failure.

Scientific Abstract:
Blood cell development is regulated through intrinsic gene regulation and local factors including the microenvironment and cytokines. The differentiation of hematopoietic stem and progenitor cells (HSPCs) into mature erythrocytes is dependent on these cytokines binding to and stimulating their cognate receptors and the signaling cascades they initiate. Many of these pathways include kinases that can diversify signals by phosphorylating multiple substrates and amplify signals by phosphorylating multiple copies of each substrate. Indeed, synthesis of many of these cytokines is regulated by a number of signaling pathways including phosphoinositide 3-kinase (PI3K)-, extracellular signal related kinases (ERK)-, and p38 kinase-dependent pathways. Therefore, kinases act both upstream and downstream of the erythropoiesis-regulating cytokines. While many of the cytokines are well characterized, the nuanced members of the network of kinases responsible for appropriate induction of, and response to, these cytokines remains poorly defined. Here, we will examine the kinase signaling cascades required for erythropoiesis and emphasize the importance, complexity, enormous amount remaining to be characterized, and therapeutic potential that will accompany our comprehensive understanding of the erythroid kinome in both healthy and diseased states.